# EAST Search History (INCLUDING INTERFERENCE)

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 5038 | 544/238 OR 544/295 OR 544/357 OR 514/252.02 OR 514/252.12 OR 514/255.05 | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT | OR | ON | 2006/10/11 07:40 |
| L2 | 101 | L1 AND (SODIUM ADJ CHANNEL) | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT | OR | ON | 2006/10/11 07:40 |
| L3 | 32 | L2 AND (AMILORIDE OR PYRAZINOYLGUANIDINE OR (PYRAZINYL ADJ GUANIDINE) OR (GUANIDINOYL ADJ PYRAZINE)) | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT | OR | ON | 2006/10/11 07:41 |

STN SEARCH TRANSCRIPT 10/828,329

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 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  FEB 27  New STN AnaVist pricing effective March 1, 2006
 NEWS  4  MAY 10  CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS  5  MAY 11  KOREAPAT updates resume
 NEWS  6  MAY 19  Derwent World Patents Index to be reloaded and enhanced
 NEWS  7  MAY 30  IPC 8 Rolled-up Core codes added to CA/CAplus and
                  USPATFULL/USPAT2
 NEWS  8  MAY 30  The F-Term thesaurus is now available in CA/CAplus
 NEWS  9  JUN 02  The first reclassification of IPC codes now complete in
                  INPADOC
 NEWS 10  JUN 26  TULSA/TULSA2 reloaded and enhanced with new search and
                  and display fields
 NEWS 11  JUN 28  Price changes in full-text patent databases EPFULL and PCTFULL
 NEWS 12  JUl 11  CHEMSAFE reloaded and enhanced
 NEWS 13  JUl 14  FSTA enhanced with Japanese patents
 NEWS 14  JUl 19  Coverage of Research Disclosure reinstated in DWPI
 NEWS 15  AUG 09  INSPEC enhanced with 1898-1968 archive
 NEWS 16  AUG 28  ADISCTI Reloaded and Enhanced
 NEWS 17  AUG 30  CA(SM)/CAplus(SM) Austrian patent law changes
 NEWS 18  SEP 11  CA/CAplus enhanced with more pre-1907 records
 NEWS 19  SEP 21  CA/CAplus fields enhanced with simultaneous left and right
                  truncation
 NEWS 20  SEP 25  CA(SM)/CAplus(SM) display of CA Lexicon enhanced
 NEWS 21  SEP 25  CAS REGISTRY(SM) no longer includes Concord 3D coordinates
 NEWS 22  SEP 25  CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
 NEWS 23  SEP 28  CEABA-VTB classification code fields reloaded with new
                  classification scheme

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:38:06 ON 11 OCT 2006

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COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

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STRUCTURE FILE UPDATES:   10 OCT 2006  HIGHEST RN 910095-75-9
DICTIONARY FILE UPDATES:  10 OCT 2006  HIGHEST RN 910095-75-9

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http://www.cas.org/ONLINE/UG/regprops.html

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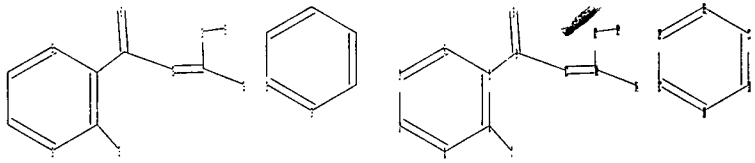

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7  8  9  10  11  12  13  14
ring nodes :
1  2  3  4  5  6  16  17  18  19  20  21
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ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  16-17  16-21  17-18  18-19  19-20  20-21
exact/norm bonds :
6-7  8-9  8-10  10-11  11-12  11-14
exact bonds :
5-8  12-13
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  16-17  16-21  17-18  18-19  19-20  20-21
isolated ring systems :
containing 1 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:CLASS
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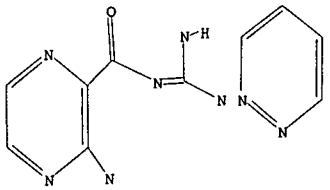

"G" RING IS
1,2 - DIAZINE

Structure attributes must be viewed using STN Express query preparation.

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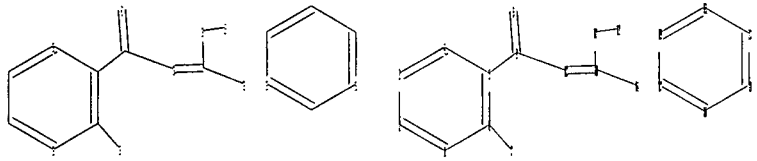

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7 8 9 10 11 12 13 14
ring nodes :
1 2 3 4 5 6 16 17 18 19 20 21
chain bonds :
5-8 6-7 8-9 8-10 10-11 11-12 11-14 12-13
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 16-17 16-21 17-18 18-19 19-20 20-21
exact/norm bonds :
6-7 8-9 8-10 10-11 11-12 11-14
exact bonds :
5-8 12-13
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 16-17 16-21 17-18 18-19 19-20 20-21
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 16:Atom 17:Atom 18:Atom 19:Atom
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L2 STRUCTURE UPLOADED

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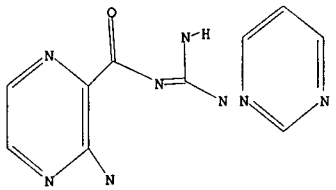
L2 HAS NO ANSWERS
L2 STR



"Q" RING IS
1,3 - DIAZINE

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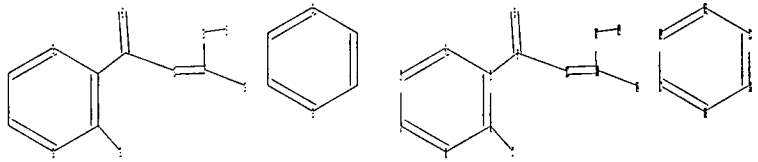

chain nodes :
7 8 9 10 11 12 13 14
ring nodes :
1 2 3 4 5 6 16 17 18 19 20 21
chain bonds :
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ring bonds :
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exact/norm bonds :
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normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 16-17 16-21 17-18 18-19 19-20 20-21
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 16:Atom 17:Atom 18:Atom 19:Atom
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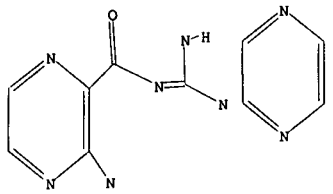
L3 STRUCTURE UPLOADED

=> D L3
L3 HAS NO ANSWERS

L3 STR



"Q" RING IS 1,4 - DIAZINE

SEARCHED ALL THREE

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -        0 TO ITERATE

100.0% PROCESSED         0 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:   ONLINE  **COMPLETE**
                         BATCH   **COMPLETE**
PROJECTED ITERATIONS:             0 TO        0
PROJECTED ANSWERS:                0 TO        0

L4             0 SEA SSS SAM L1

=> S L2
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SEARCH TIME: 00.00.01

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PROJECTED ITERATIONS:             3 TO      163
PROJECTED ANSWERS:                0 TO        0

L5             0 SEA SSS SAM L2

=> S L3
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100.0% PROCESSED         3 ITERATIONS                              2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:   ONLINE  **COMPLETE**
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PROJECTED ITERATIONS:             3 TO      163
PROJECTED ANSWERS:                2 TO      124

L6             2 SEA SSS SAM L3

=> S L1 SSS FULL
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100.0% PROCESSED        12 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

L7             0 SEA SSS FUL L1

=> S L2 SSS FULL
FULL SEARCH INITIATED 08:39:57 FILE 'REGISTRY'
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100.0% PROCESSED        71 ITERATIONS                             18 ANSWERS
SEARCH TIME: 00.00.01

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=> S L3 SSS FULL
FULL SEARCH INITIATED 08:40:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -       71 TO ITERATE

100.0% PROCESSED        71 ITERATIONS                             20 ANSWERS
SEARCH TIME: 00.00.01

L9            20 SEA SSS FUL L3

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                                              ENTRY    SESSION
FULL ESTIMATED COST                           500.82     501.03

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=> S L8 OR L9
             7 L8
             4 L9
L10         11 L8 OR L9

=> D 1-11 IBIB ABS HITSTR

L10  ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2005:346797  CAPLUS
DOCUMENT NUMBER:         142:411366
TITLE:                   Preparation of pyridazinylcarbonyl-substituted ureas
                         used for reducing risk of infection from pathogens
INVENTOR(S):             Johnson, Michael R.; Hopkins, Samuel E.
```

PATENT ASSIGNEE(S): Parion Sciences, Inc., USA
SOURCE: PCT Int. Appl., 218 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2005034847 | A2 | 20050421 | WO 2004-US26963 | 20040819 |
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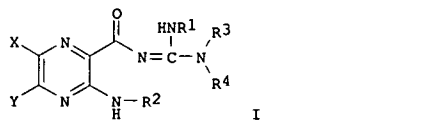
| WO 2004-US26963 | W | 20040819 |

OTHER SOURCE(S): MARPAT 142:411366
GI



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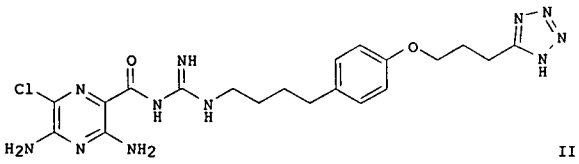


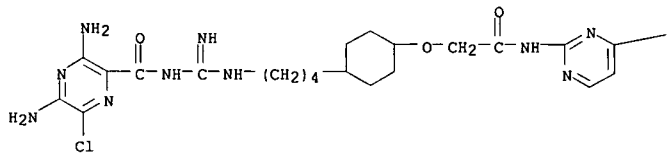
II

AB Title compds. I [X = H, halo, CF3, etc.; Y = H, OH, SH, etc.; R1 = H, alkyl; R2 = alkoxy, etc.; R3-4 = H, alkyl, OH, alkyl, Ph, etc.] are prepared for instance, II is prepared in 4 steps from [4-(4-hydroxyphenyl)butyl]carbamic acid benzyl ester (preparation given), 4-bromobutyronitrile and 1-(3,5-diamino-6-chloropyrazine-2-carbonyl)-2-methylisothiourea•HI. II has EC50 = 25 nM in a sodium channel blocker assay. I are useful for prophylactic treatment to one or more members of a population at risk of exposure to or already exposed to one or more airborne pathogens, either from natural sources or from intentional release of pathogens into the environment.

IT *845753-79-9P 847200-87-7P 847200-90-2P*
*847200-91-3P*
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridazinylcarbonyl-substituted ureas used for reducing risk of infection from pathogens)

RN 845753-79-9 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(4-amino-2-pyrimidinyl)amino]-2-oxoethoxy]cyclohexyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)

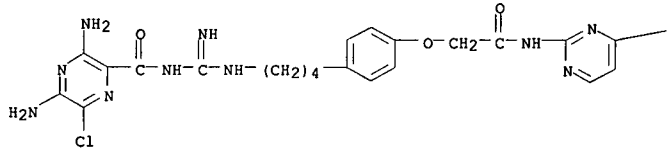
PAGE 1-A



PAGE 1-B

RN 847200-87-7 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(4-amino-2-pyrimidinyl)amino]-2-oxoethoxy]phenyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)

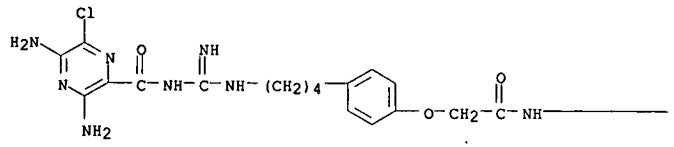
PAGE 1-A



PAGE 1-B

RN 847200-90-2 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(6-amino-1H-purin-2-yl)amino]-2-oxoethoxy]phenyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)

PAGE 1-A



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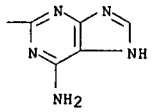
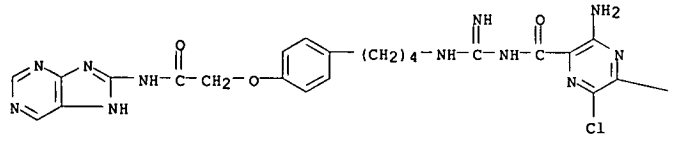


RN 847200-91-3 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[imino[[4-[4-[2-oxo-2-(1H-purin-8-ylamino)ethoxy]phenyl]butyl]amino]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

L10 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:177896 CAPLUS
DOCUMENT NUMBER: 142:280225
TITLE: Preparation of capped aminopyrazinoylguanidines as sodium channel blockers

INVENTOR(S): Johnson, Michael R.; Molino, Bruce F.; Zhang, Jianzhong; Sargent, Bruce J.
PATENT ASSIGNEE(S): Parion Sciences, Inc., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005018644 | A1 | 20050303 | WO 2004-US26885 | 20040818 |
| WO 2005018644 | B1 | 20050512 | | |
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| CA 2534682 | AA | 20050303 | CA 2004-2534682 | 20040818 |
| US 2005080091 | A1 | 20050414 | US 2004-920410 | 20040818 |
| US 7064129 | B2 | 20060620 | | |
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| US 2006052394 | A1 | 20060309 | US 2005-211422 | 20050826 |
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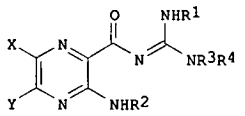
| US 2006205738 | A1 | 20060914 | US 2005-211707 | 20050826 |

PRIORITY APPLN. INFO.:
US 2003-495725P P 20030818
US 2004-920410 A1 20040818
WO 2004-US26885 W 20040818

OTHER SOURCE(S): MARPAT 142:280225
GI



I

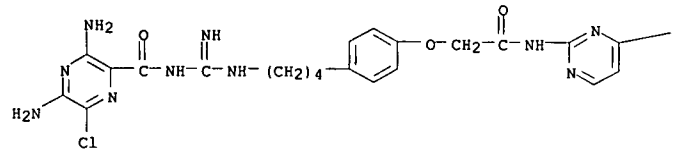
AB Title compds. [I; X = H, halo, CF3, alkyl, (substituted) Ph, etc.; Y = H, OH, SH, alkoxy, alkylthio, halo, alkyl, (substituted) aryl, etc.; R1 = H, alkyl; R2 = R7, (CH2)mOR8, (CH2)mNR7R10, (CH2CH2O)mR8, etc.; m = 1-7; R3, R4 = H, alkyl, hydroxyalkyl, Ph, phenylalkyl, naphthylalkyl, pyridylalkyl, etc.; R7 = H, alkyl, (substituted) Ph, etc.; R8 = H, alkyl, 2-tetrahydropyranyl, glucuronide, etc.; R10 = H, SO2Me, COR13, CO2R13, etc.; R13 = H, R7, R10, etc.; with provisos], were prepared Thus, [4-(4-hydroxyphenyl)butyl]carbamic acid benzyl ester in EtOH at 70° was treated with oxiranylmethanol over 4 h to give 4.6% [4-[4-[3-(2,3-dihydroxypropoxy)-2-hydroxypropoxy]phenyl]butyl]carbamic acid benzyl ester. This was hydrogenolyzed in EtOH over Pd/C to give 51% 3-[3-[4-(4-aminobutyl)phenoxy]-2-hydroxypropoxy]propane-1,2-diol. The

latter was stirred with Et3N and 1-(3,5-diamino-6-chloropyrazine-2-carbonyl)-2-methylisothiourea hydroiodide in EtOH at 65° to give 36% N-(3,5-diamino-6-chloropyrazine-2-carbonyl)-N'-[4-[4-[3-(2,3-dihydroxypropoxy)-2-hydroxypropoxy]phenyl]butyl]guanidine (PSA 15143). The latter showed Na channel blocking activity with EC50 = 7 nM.

IT *847200-87-7P 847200-90-2P 847200-91-3P*
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of aminopyrazinoylguanidines as sodium channel blockers)

RN 847200-87-7 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(4-amino-2-pyrimidinyl)amino]-2-oxoethoxy]phenyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)

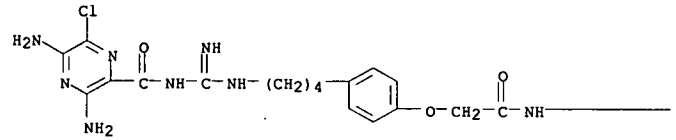
PAGE 1-A



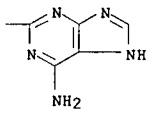
PAGE 1-B

RN 847200-90-2 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(6-amino-1H-purin-2-yl)amino]-2-oxoethoxy]phenyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)

PAGE 1-A

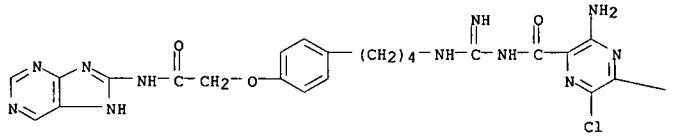


PAGE 1-B



RN 847200-91-3 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[imino[[4-[4-[2-oxo-2-(1H-purin-8-ylamino)ethoxy]phenyl]butyl]amino]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:158635 CAPLUS
DOCUMENT NUMBER: 142:261557
TITLE: Preparation of cyclic pyrazinoylguanidine sodium channel blockers
INVENTOR(S): Johnson, Michael R.
PATENT ASSIGNEE(S): Parion Sciences, Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

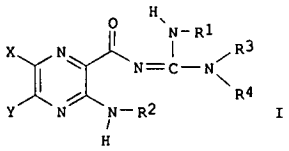
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005016879 | A2 | 20050224 | WO 2004-US26880 | 20040818 |
| WO 2005016879 | A3 | 20050602 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| AU 2004264441 | A1 | 20050224 | AU 2004-264441 | | 20040818 |
| CA 2534569 | AA | 20050224 | CA 2004-2534569 | | 20040818 |
| US 2005059676 | A1 | 20050317 | US 2004-920353 | | 20040818 |
| EP 1670474 | A2 | 20060621 | EP 2004-801870 | | 20040818 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | | |
| US 2006205738 | A1 | 20060914 | US 2005-211707 | | 20050826 |
| PRIORITY APPLN. INFO.: | | | US 2003-495720P | P | 20030818 |
| | | | US 2004-920410 | A3 | 20040818 |
| | | | WO 2004-US26880 | W | 20040818 |

OTHER SOURCE(S): CASREACT 142:261557; MARPAT 142:261557
GI



I

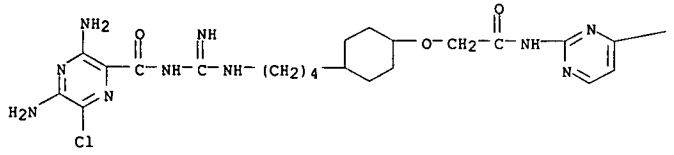
AB The title compds. I [X = halo, etc.; Y = H, hydroxyl, etc.; R1 = H, alkyl; R2 = R7, etc.; R3, R4 = H, alkyl, etc.; R7 = (un)substituted Ph, etc], useful as sodium channel blockers (no data), are prepared Thus, N-(3,5-diamino-6-chloropyrazine-2-carbonyl)-N'-[4-[1-(2-hydroxyethyl)piperidin-4-yl]butyl]guanidine dihydrochloride was prepared in a multistep process starting from 4-(piperidin-4-yl)butyric acid HCl salt.

IT *845753-79-9P*
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic pyrazinoylguanidine sodium channel blockers)

RN 845753-79-9 CAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-N-[[[4-[4-[2-[(4-amino-2-pyrimidinyl)amino]-2-oxoethoxy]cyclohexyl]butyl]amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)









L10 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:63982 CAPLUS
DOCUMENT NUMBER: 134:115971
TITLE: Pyrazinoylguanidine derivatives as conjugates of sodium channel blockers and methods of using the same for hydrating mucosal surfaces
INVENTOR(S): Boucher, Richard C., Jr.
PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

THIS IS PRIOR ART

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2001005773 | A1 | 20010125 | WO 2000-US19775 | | 20000719 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2378181 | AA | 20010125 | CA 2000-2378181 | | 20000719 |
| EP 1196396 | A1 | 20020417 | EP 2000-948820 | | 20000719 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| US 6475509 | B1 | 20021105 | US 2000-618978 | | 20000719 |
| NZ 516595 | A | 20030725 | NZ 2000-516595 | | 20000719 |
| JP 2004513870 | T2 | 20040513 | JP 2001-511434 | | 20000719 |
| AU 774865 | B2 | 20040708 | AU 2000-62262 | | 20000719 |
| ZA 2002000129 | A | 20030407 | ZA 2002-129 | | 20020107 |
| NO 2002000242 | A | 20020319 | NO 2002-242 | | 20020116 |
| US 2002165239 | A1 | 20021107 | US 2002-121913 | | 20020412 |
| US 6607741 | B2 | 20030819 | | | |
| US 2002158255 | A1 | 20030902 | US 2002-121917 | | 20020412 |
| US 6613345 | B2 | 20030902 | | | |
| PRIORITY APPLN. INFO.: | | | US 1999-144479P | P | 19990719 |
| | | | US 2000-618978 | A | 20000719 |
| | | | WO 2000-US19775 | W | 20000719 |

OTHER SOURCE(S): MARPAT 134:115971
GI

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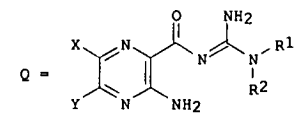
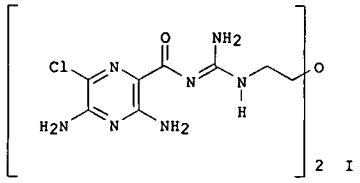




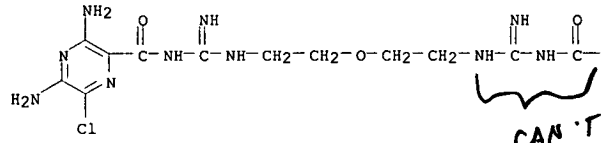
AB Compds. of the general formula P1-L-P2 [L = linker; P1 = a pyrazinoylguanidine sodium channel blocker; P2 = a dinucleotide, a pyrazinoylguanidine sodium channel blocker and/or a P2Y2 receptor agonist; P1 and P2 may be independently Q wherein X = halo, alkyl, cycloalkyl, (un)substituted Ph, alkylthio, alkylsulfonyl, oxyalkylthio, oxyalkylsulfonyl, phenylalkylthio and phenylalkylsulfonyl; Y = OH, mercapto, alkyloxy, alkylthio, Cl, alkyl, cycloalkyl, Ph and amino derivs.; R1 and R2 are independently selected from H, alkyl, hydroxyalkyl, (un)substituted phenylalkyl, etc.; L = alkyl, hydroxyalkyl, (un)substituted arylalkyl, etc.] are prepared and disclosed as conjugates of sodium channel blockers. Thus, I was prepared via substitution reactions of N-Cbz-1-(3,5-diamino-6-chloropyrazinoyl)-2-methylpseudothiourea with 1,5-diamino-3-oxapentane. I possessed an IC50 value of 1275 nM in an assay for Na+ channel subunit expression in Xenopus oocytes, and was found to absorb into cells less rapidly than amiloride. Pharmaceutical formulations containing the disclosed compds. and methods of use thereof to hydrate mucosal surfaces such as airway mucosal surfaces are also disclosed.

IT *321554-65-8P 321554-67-0P 321554-68-1P*
*321554-69-2P 321554-70-5P 321554-71-6P*
*321554-72-7P 321554-73-8P*
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazinoylguanidine derivs. as conjugates of sodium channel blockers used for hydration of mucosal surfaces)

RN 321554-65-8 CAPLUS
CN Pyrazinecarboxamide, N,N'-[oxybis(2,1-ethanediyliminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)

BIS-AMILORIDE COMPDS:

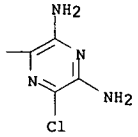
PAGE 1-A



CAN'T BE IN (A) LINKER

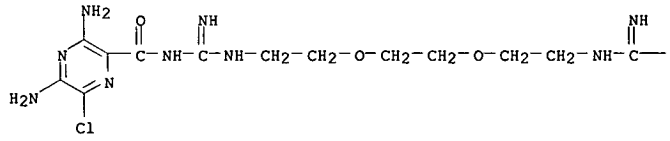
●2 HBr

PAGE 1-B



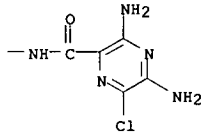
RN 321554-67-0 CAPLUS
CN Pyrazinecarboxamide, N,N'-(1,12-diimino-5,8-dioxa-2,11-diazadodecane-1,12-diyl)bis[3,5-diamino-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

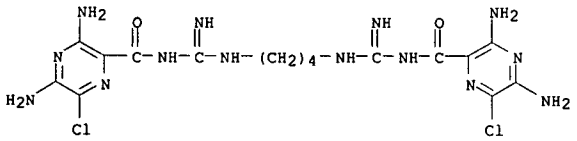


●2 HCl

PAGE 1-B

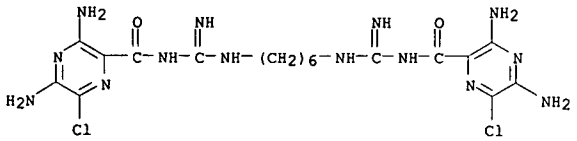


RN 321554-68-1 CAPLUS
CN Pyrazinecarboxamide, N,N'-[1,4-butanediylbis(iminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

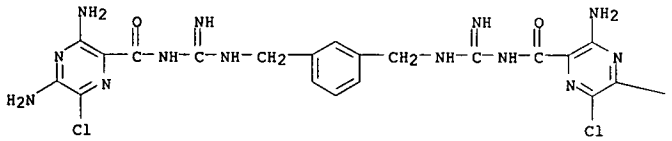
RN 321554-69-2 CAPLUS
CN Pyrazinecarboxamide, N,N'-[1,6-hexanediylbis(iminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

RN 321554-70-5 CAPLUS
CN Pyrazinecarboxamide, N,N'-[1,3-phenylenebis(methyleneiminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)

PAGE 1-A

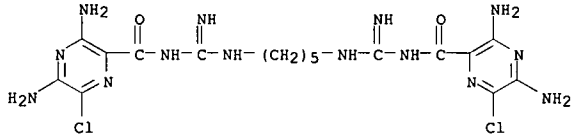


●2 HBr

PAGE 1-B

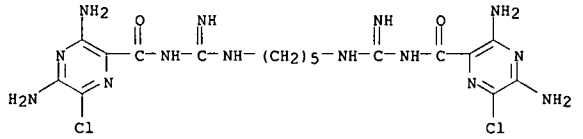
NH2

RN 321554-71-6 CAPLUS
CN Pyrazinecarboxamide, N,N'-[1,5-pentanediylbis(iminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

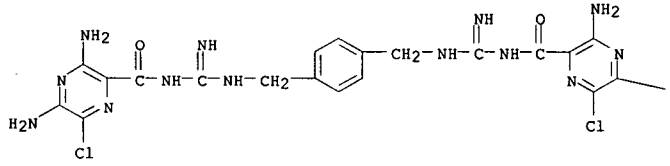
RN 321554-72-7 CAPLUS
CN Pyrazinecarboxamide, N,N'-[1,5-pentanediylbis(iminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

RN 321554-73-8 CAPLUS
CN Pyrazinecarboxamide, N,N'-[1,4-phenylenebis(methyleneiminocarbonimidoyl)]bis[3,5-diamino-6-chloro-, dihydrobromide (9CI) (CA INDEX NAME)

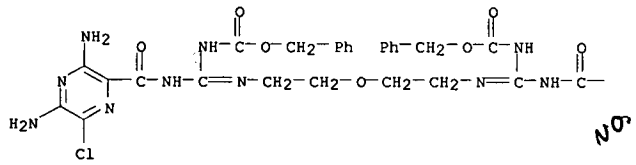
PAGE 1-A



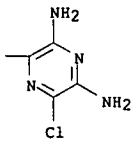
●2 HBr

IT *321554-75-0P*
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrazinoylguanidine derivs. as conjugates of sodium channel blockers used for hydration of mucosal surfaces)
RN 321554-75-0 CAPLUS
CN 7-Oxa-2,4,10,12-tetraazatrideca-2,10-dienedioic acid, 3,11-bis[[(3,5-diamino-6-chloropyrazinyl)carbonyl]amino]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)









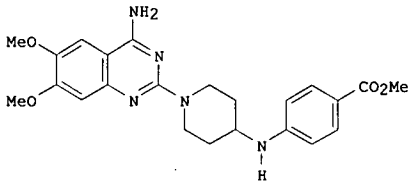
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:855763 CAPLUS
DOCUMENT NUMBER: 134:29423
TITLE: Preparation of [(quinazolinylpiperidinyl)amino]benzoates and analogs as bactericides
INVENTOR(S): Kung, Pei-Pei; Cook, Phillip Dan; Guinosso, Charles John
PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
SOURCE: U.S., 22 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6156758 | A | 20001205 | US 1999-391843 | 19990908 |
| PRIORITY APPLN. INFO.: | | | US 1999-391843 | 19990908 |
| OTHER SOURCE(S): | MARPAT 134:29423 | | | |

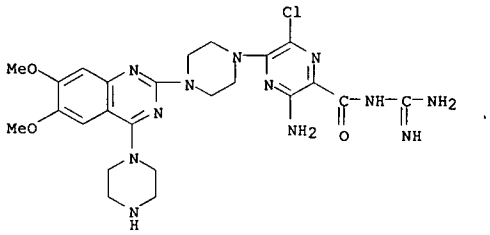
GI



II

AB RZ(NR4)nZCO2R1 [I; R = (un)substituted 2-quinazolinyl; R1 = OH, (ar)alkoxy, aryloxy, etc.; R4 = H, alkyl, acyl; Z = piperidine- or piperazine-1,4-diyl; Z1 = (un)substituted 1,4-phenylene, -pyridine-2,5- or -5,2-diyl, -pyrazine-2,5-diyl; n = 0 or 1] were prepared Thus, Me 3-amino-5,6-dichloro-2-pyrazinecarboxylate was condensed with 1-protected-4-aminopiperidine and the deprotected product condensed with 4-amino-2-chloro-6,7-dimethoxyquinazoline to give title compound II. Data for biol. activity of I were given.

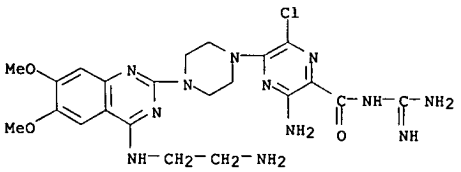
IT *310901-30-5P 310901-33-8P*
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of [(quinazolinylpiperidinyl)amino]benzoates and analogs as bactericides)
RN 310901-30-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-[6,7-dimethoxy-4-(1-piperazinyl)-2-quinazolinyl]-1-piperazinyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 310901-33-8 CAPLUS

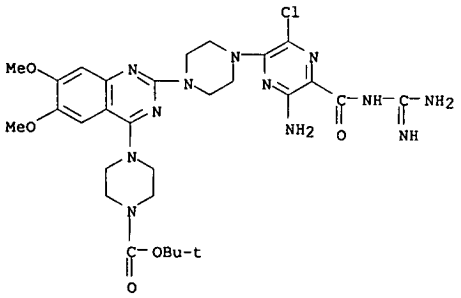
CN Pyrazinecarboxamide, 3-amino-5-[4-[4-[(2-aminoethyl)amino]-6,7-dimethoxy-2-quinazolinyl]-1-piperazinyl]-N-(aminoiminomethyl)-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



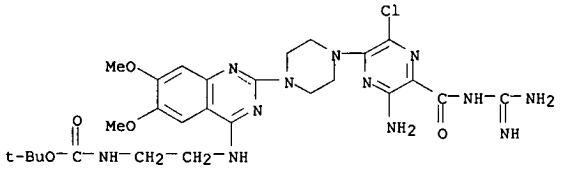
●2 HCl

IT *310901-41-8P 310901-46-3P*
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [(quinazolinylpiperidinyl)amino]benzoates and analogs as bactericides)

RN 310901-41-8 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[2-[4-[6-amino-5-[[(aminoiminomethyl)amino]carbonyl]-3-chloropyrazinyl]-1-piperazinyl]-6,7-dimethoxy-4-quinazolinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 310901-46-3 CAPLUS
CN Carbamic acid, [2-[[2-[4-[6-amino-5-[[(aminoiminomethyl)amino]carbonyl]-3-chloropyrazinyl]-1-piperazinyl]-6,7-dimethoxy-4-quinazolinyl]amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:789190 CAPLUS
DOCUMENT NUMBER: 123:198830
TITLE: Preparation of amidinocarbamoylpyrazines as drugs.
INVENTOR(S): Roos, Otto; Speck, Georg; Loesel, Walter; Arndts, Dietrich
PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 4337609 | A1 | 19950511 | DE 1993-4337609 | 19931104 |
| CA 2175837 | AA | 19950511 | CA 1994-2175837 | 19941031 |
| WO 9512592 | A1 | 19950511 | WO 1994-EP3580 | 19941031 |
| W: AM, AU, BG, CA, CN, CZ, FI, GE, HU, JP, KR, KZ, LT, LV, NO, NZ, PL, RO, RU, SI, SK, UA, US, UZ, VN | | | | |
| RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9479936 | A1 | 19950523 | AU 1994-79936 | 19941031 |
| AU 690588 | B2 | 19980430 | | |
| EP 726899 | A1 | 19960821 | EP 1994-931018 | 19941031 |
| EP 726899 | B1 | 20000119 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| CN 1134151 | A | 19961023 | CN 1994-194016 | 19941031 |
| JP 09505035 | T2 | 19970520 | JP 1994-513010 | 19941031 |
| AT 188965 | E | 20000215 | AT 1994-931018 | 19941031 |
| ES 2140565 | T3 | 20000301 | ES 1994-931018 | 19941031 |
| ZA 9408669 | A | 19950704 | ZA 1994-8669 | 19941103 |
| GR 3033034 | T3 | 20000831 | GR 2000-400720 | 20000322 |

PRIORITY APPLN. INFO.: DE 1993-4337609 A 19931104
WO 1994-EP3580 W 19941031

OTHER SOURCE(S): MARPAT 123:198830
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

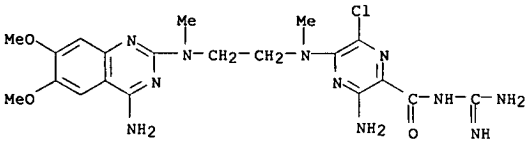
AB Title compds. [I; R1 = H, (hydroxy-substituted, O-interrupted) alkyl, alkenyl, alkynyl, Ph, cycloalkyl, etc.; R2 = Q1, Q2, etc.; R1R2N = Q3, etc.], were prepared as inhibitors of Na+/H+ and Na+/Li+ exchange useful as antihypertensives, antiischemics, mucolytics, diuretics, anticancer

agents, etc. (no data). Thus, N-(4-amino-6,7-dimethoxy-2-quinazolinyl)-N,N'-dimethyl-1,2-diaminoethane, Me 3-amino-5,6-dichloropyrazine-2-carboxylate, and Et3N were heated in Me2SO at 80° to give a residue which was stirred with guanidine hydrochloride in methanolic NaOMe to give Me 3-amino-6-chloro-5-[2-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-(N,N'-dimethyl-1,2-dimaminoethyl)]pyrazine-2-carboxylate. This was refluxed in DMF and the residue was treated with HCl in EtOH to give title compound (II).

IT *167684-27-7P*
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidinocarbamoylpyrazines as drugs)

RN 167684-27-7 CAPLUS

CN Pyrazinecarboxamide, 3-amino-5-[[2-[(4-amino-6,7-dimethoxy-2-quinazolinyl)methylamino]ethyl]methylamino]-N-(aminoiminomethyl)-6-chloro-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L10 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:449413 CAPLUS
DOCUMENT NUMBER: 119:49413
TITLE: New pyrazine derivatives, their preparation and their use as ingredients in drugs
INVENTOR(S): Koeppe, Herbert; Speck, Georg; Stockhaus, Klaus
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim KG
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

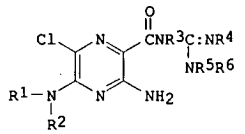
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9304048 | A1 | 19930304 | WO 1992-EP1738 | 19920731 |
| W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG | | | | |
| DE 4127026 | A1 | 19930218 | DE 1991-4127026 | 19910816 |
| DE 4130461 | A1 | 19930318 | DE 1991-4130461 | 19910913 |
| AU 9223870 | A1 | 19930316 | AU 1992-23870 | 19920731 |
| AU 669122 | B2 | 19960530 | | |
| EP 598770 | A1 | 19940601 | EP 1992-916697 | 19920731 |
| EP 598770 | B1 | 19971015 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| JP 06509798 | T2 | 19941102 | JP 1992-504057 | 19920731 |
| NO 9400523 | A | 19940215 | NO 1994-523 | 19940215 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| DE 1991-4127026 | A | 19910816 |
| DE 1991-4130461 | A | 19910913 |
| WO 1992-EP1738 | A | 19920731 |

OTHER SOURCE(S): CASREACT 119:49413; MARPAT 119:49413

GI



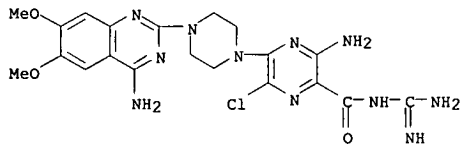
I

AB A process for the preparation of pyrazine derivative I where R1 = H or alkyl, R2 =
functionalized alkyl moiety, R3, R5 = H and R4, R6 = H, Me, Et, Bu, benzyl was accomplished by conventional methods. E.g., reaction of 4.44 g of Me 3-amino-5,6-dichloropyrazine-2-carboxylate and 3.6 g of 2-amino-1-(2,6-dimethylphenoxy)propane with 2.2 g Et3N in 40 mL anhydrous DMF gave an intermediate pyrazinecarboxylic acid ester which underwent subsequent ammonolysis in 50 mL MeOH and 80mL of methanolic guanidine solution and eluted on silica gel by AcOH:i-PrOH:NH3 eluent to give N-amidino-3-amino-6-chloro-5-(2-[1-(2,6-dimethylphenoxy)]propylamino)pyrazine-2-carboxamide-hydrochloride. The products are suitable for use as active ingredients in drugs (no data).

IT *147894-06-2P 147894-29-9P 147932-13-6P*
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 147894-06-2 CAPLUS

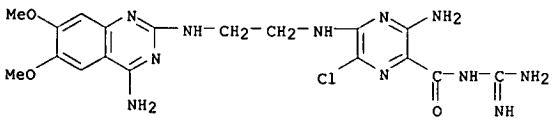
CN Pyrazinecarboxamide, 3-amino-5-[4-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl]-N-(aminoiminomethyl)-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

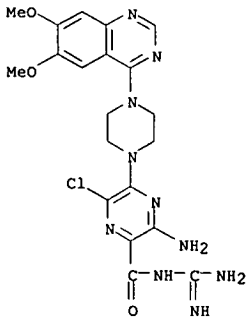
RN 147894-29-9 CAPLUS

CN Pyrazinecarboxamide, 3-amino-5-[[2-[(4-amino-6,7-dimethoxy-2-quinazolinyl)amino]ethyl]amino]-N-(aminoiminomethyl)-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 147932-13-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(6,7-dimethoxy-4-quinazolinyl)-1-piperazinyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L10 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:408831 CAPLUS
DOCUMENT NUMBER: 119:8831
TITLE: Preparation of 2-guanidinocarbonyl-3,5-diamino-6-chloropyrazines as drugs
INVENTOR(S): Koeppe, Herbert; Speck, Georg; Stockhaus, Klaus
PATENT ASSIGNEE(S): Boehringer Ingelheim KG, Germany
SOURCE: Ger. Offen., 19 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

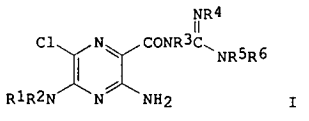
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 4127026 | A1 | 19930218 | DE 1991-4127026 | 19910816 |
| WO 9304048 | A1 | 19930304 | WO 1992-EP1738 | 19920731 |

W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG

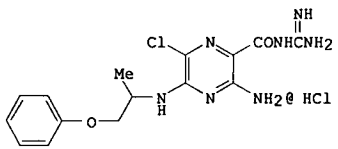
| | | | | |
|---|---|---|---|---|
| AU 9223870 | A1 | 19930316 | AU 1992-23870 | 19920731 |
| AU 669122 | B2 | 19960530 | | |
| EP 598770 | A1 | 19940601 | EP 1992-916697 | 19920731 |
| EP 598770 | B1 | 19971015 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| JP 06509798 | T2 | 19941102 | JP 1992-504057 | 19920731 |
| HU 67661 | A2 | 19950428 | HU 1994-430 | 19920731 |
| CZ 280760 | B6 | 19960417 | CZ 1994-337 | 19920731 |
| AT 159250 | E | 19971115 | AT 1992-916697 | 19920731 |
| ES 2108129 | T3 | 19971216 | ES 1992-916697 | 19920731 |
| RU 2124008 | C1 | 19981227 | RU 1994-15265 | 19920731 |
| ZA 9206132 | A | 19930331 | ZA 1992-6132 | 19920814 |
| NO 9400523 | A | 19940215 | NO 1994-523 | 19940215 |

PRIORITY APPLN. INFO.:
DE 1991-4127026 A 19910816
DE 1991-4130461 A 19910913
WO 1992-EP1738 A 19920731

OTHER SOURCE(S): MARPAT 119:8831
GI

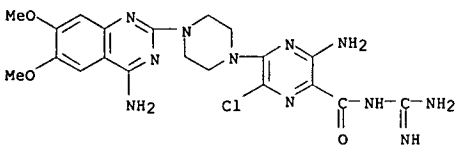


I



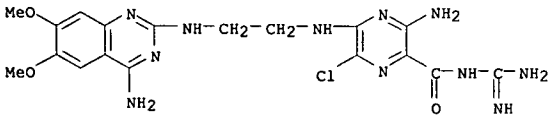
II

AB Title compds. [I; R1 = H, alkyl; R2 = morpholino, (substituted) alkyl, 4-piperidinyl, amidino; R1R2N = (substituted) piperidinyl, piperazinyl; R3-R6 = H, alkyl, PhCH2], effective inhibitors of Na+/H+ and Na+/Li+ exchange useful as antihypertensives, mucolytics, diuretics, neoplasm inhibitors, and platelet activating factor antagonists (no data), are prepared Thus, Me 3-amino-5,6-dichloropyrazine-2-carboxylate, 2-amino-1-(2,6-dimethylphenoxy)propane, and Et3N were heated in DMF at 95-100° for 1.5 h to give Me 3-amino-6-chloro-5-[2-[1-(2,6-dimethylphenoxy)]propylamino]pyrazine-2-carboxylate. This was heated with guanidine in MeOH to give title compound II.
IT *147894-06-2P 147894-29-9P 147932-13-6P*
*147932-29-4P*
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)
RN 147894-06-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-[4-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl]-N-(aminoiminomethyl)-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



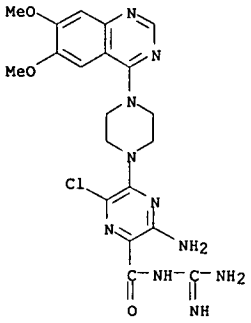
●2 HCl

RN 147894-29-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-[[2-[(4-amino-6,7-dimethoxy-2-quinazolinyl)amino]ethyl]amino]-N-(aminoiminomethyl)-6-chloro-, dihydrochloride (9CI) (CA INDEX NAME)



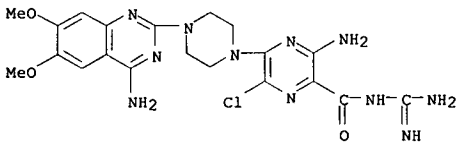
●2 HCl

RN 147932-13-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-6-chloro-5-[4-(6,7-dimethoxy-4-quinazolinyl)-1-piperazinyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 147932-29-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-[4-(4-amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl]-N-(aminoiminomethyl)-6-chloro- (9CI) (CA INDEX NAME)

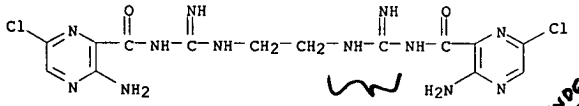


L10 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:37949 CAPLUS
DOCUMENT NUMBER: 66:37949
TITLE: Pyrazinoylguanidines
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: Neth. Appl., 17 pp.
CODEN: NAXXAN
DOCUMENT TYPE: Patent
LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| NL 6504569 | | 19661010 | NL 1965-4569 | 19650409 |
| FR 1479232 | | | FR | |
| FR 4498 | | | FR | |

OTHER SOURCE(S): MARPAT 66:37949
GI For diagram(s), see printed CA Issue.
AB The title compds. I (X = halogen; R1-4 = H or alkyl) are prepared by reaction of 3-(NRR-substituted)-6-(X-substituted)-pyrazine-2-carboxylic acid esters (II) with guanidines H2NC-(:NR2)NR3R4 (III). Thus, through 1.5 g. 3-(methylamino)-pyrazine-2-carboxylic acid in 250 ml. MeOH was passed HCl gas, the solution evaporated, neutralized with NaHCO3 solution, treated with 0.5 cc. Br, and filtered to obtain 1.7 g. Me ester of 3-(methylamino)-6-bromopyrazine-2-carboxylic acid (IV), m. 181.5-3.5°(iso-PrOH). Na (0.69 g.) was dissolved in 90 ml. MeOH; to the cold solution 3.01 g. dry powdered guanidine-HCl was added and the mixture refluxed 30 min. and filtered; to the filtrate 2 g. IV was added to give 1.1 g. [3-methylamino)-6-bromo-2-purazinoyl]-guanidine, m. 230.5-1.5°. To 23 g. Me ester of 3-amino-6-bromopyrazine-2-carboxylic acid in 40 cc. AcOH and 114 cc. 48% HBr at 5-10° a solution of 15 cc. Br in 40 cc. AcOH was added and the mixture treated at 0-5° with 17.4 g. NaNO2 in 30 cc. H2O in 1.5 hrs. To this stirred mixture at 20° 200 ml. 10N NaOH and saturated NaHSO3 solution was added to give 17.4 g. Me ester of 3,6-dibromopyrazine-2-carboxylic acid (V), m. 66-8° (aqueous EtOH). V (6 g.) and piperidine 30 min. at 25° gave the 3-piperidino derivative of V, m. 88-9°; its guanidino derivative m. 220-2°. Me2NH (15 g.) and 6 g. V gave the 3-Me2N derivative of V, m. 105-8°; its guanidino derivative m. 216-18°. The Me ester of 3-bromo-6-chloropyrazine-2-carboxylic acid, m. 35-6° gave the 3-[2-(dimethylamino)ethylamino] derivative, m. 105-8°; its guanidine derivative m. 221-13°. Ethylenebis[3-(3-amino-6-chloro-2-pyrazinoyl)guanidine]-2HCl, m. 323°. Treatment of β-amino-6-chloro-2-pyrazinoyl)guanidine with AcCl gave the 2,3-diacetylguanidine derivative, m. 187.5-8.5°; the analogous 2,3-di-Bz derivative m. 215-17°. [TABLE OMITTED] Other I (R = R1 = H) given in the table were prepared The compds. are diuretics.
IT *13301-07-0P*

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 13301-07-0 CAPLUS
CN Pyrazinecarboxamide, N,N'-[ethylenebis(iminoimidocarbonyl)]bis[3-amino-6-chloro-, dihydrochloride (8CI) (CA INDEX NAME)



●2 HCl

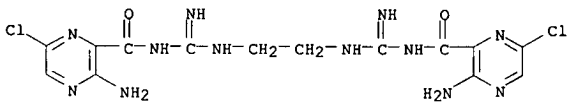
NOT IN Cl 82 (THE INDEPENDENT CL.) GUANIDYL NOT PERMITTED IN (A) AS A LINKER

L10 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:10961 CAPLUS
DOCUMENT NUMBER: 66:10961
TITLE: Pyrazinoylguanidines
INVENTOR(S): Cragoe, Edward J., Jr.; Southwick, Philip L.
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: Belg., 25 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| BE 662507 | | 19651004 | | |
| GB 1095792 | | | GB | |
| US 3240780 | | 19660315 | US 1963-332901 | 19631223 |
| PRIORITY APPLN. INFO.: | | | US | 19631223 |

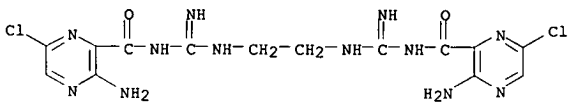
GI For diagram(s), see printed CA Issue.
AB Pyrazinoylguanidines (I) having diuretic and natriuretic properties are prepared Thus, 1.5 g. 3-methylaminopyrazinoic acid in 250 ml. MeOH is treated with gaseous HCl until saturation, the solution refluxed 2 hrs. and evaporated to dryness, saturated NaHCO3 aqueous solution added until pH 7 is reached, and 0.5 ml. Br added to give 1.7 g. Me 3-methylamino-6-bromopyrazinoate (III), m. 181.5-3.5° (iso-PrOH). Na (0.69 g.) is dissolved in 90 ml. MeOH, 3.02 g. guanidine hydrochloride added, the solution refluxed 30 min., precipitated NaCl filtered off, 2 g. III added, and the mixture heated for a short period and kept 1 hr. at room temperature to give 1.1 g. IV. The following compds. are similarly prepared (m.p. given): Me 3,6-dibromopyrazinoate, 66-8°; Me 3-piperidino-6-bromopyrazinoate, 88-90°; Me 3-dimethylamino-6-bromopyrazinoate, 80-2; Me 3-bromo-6-chloropyrazinoate, 35-6°; Me 3-(2-dimethylaminoethylamino)-6-chloropyrazinoate, 105-8°; ethylenebis[3-(3-amino-6-chloro-2-pyrazinoyl)guanidine],-(HCl salt m. 323°); 1-(3-amino-6-chloropyrazinoyl)-2,3-diacetylguanidine -; 1-(3-amino-6-chloropyrazinoyl)-2,3-dibenzoylguanidine, 215-17°; 1-(3-metnylamino-6-trifluoromethylpyrazinoyl)-3-benzylguanidine, -; 1-(3-amino-6-trifluoromethylpyrazinoyl)-2,3-diacetylguanidine, -; 1-(3-amino-6-trifluoromethylpyrazinoyl)-3,3-dimethylguanidine, -. Similarly prepared were the tabulated I. [TABLE OMITTED]
IT *13301-07-0P*

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 13301-07-0 CAPLUS
CN Pyrazinecarboxamide, N,N'-[ethylenebis(iminoimidocarbonyl)]bis[3-amino-6-chloro-, dihydrochloride (8CI) (CA INDEX NAME)



●2 HCl

L10 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:463090 CAPLUS
DOCUMENT NUMBER: 63:63090
ORIGINAL REFERENCE NO.: 63:11561e-f
TITLE: Pyrazine diuretics. I. N-Amidino-3-amino-6-halopyrazinecarboxamides
AUTHOR(S): Bicking, John B.; Mason, James W.; Woltersdorf, Otto W., Jr.; Jones, James H.; Kwong, Sara F.; Robb, Charles M.; Cragoe, Edward J., Jr.
CORPORATE SOURCE: Merck & Co., Inc., West Point, PA
SOURCE: Journal of Medicinal Chemistry (1965), 8(5), 638-42
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 63:63090
AB A series of N-amidino-3-amino-6-halopyrazinecarboxamides was prepared principally by the reaction of Me 3-amino-6-halopyrazinecarboxylates with guanidine or substituted guanidines. A number of these compds. reverse the electrolyte excretion effects of deoxycorticosterone in the adrenalectomized rat and cause natriuresis in the intact rat and dog while leaving unaffected or even repressing K+ excretion.
IT *96878-31-8*, Pyrazinecarboxamide, N,N'-[ethylenebis[imino(imidocarbonyl)]]bis[3-amino-6-chloro-, hydrochloride (preparation of)
RN 96878-31-8 CAPLUS
CN Pyrazinecarboxamide, N,N'-[ethylenebis[imino(imidocarbonyl)]]bis[3-amino-6-chloro-, hydrochloride (7CI) (CA INDEX NAME)



●x HCl

=> LOG HOLD
COST IN U.S. DOLLARS SINCE FILE TOTAL

∴ NO PRIOR ART.

| | ENTRY | SESSION |
|---|---|---|
| FULL ESTIMATED COST | 56.67 | 557.70 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -8.25 | -8.25 |

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:40:33 ON 11 OCT 2006